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Doc Code: AP.PRE.REQ

PTO/SB/33 (07-05)
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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): DEX-0176

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Application Number	Filed
09/787,844	August 6, 2001

First Named Inventor: Ali et al.

Art Unit	Examiner
1642	Yu, Misook

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

I am the

- ☐ applicant/inventor.
- ☐ assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- ☒ attorney or agent of record. Registration number 38,350
- ☐ attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

Signature

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Typed or printed name

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Telephone number

February 5, 2008
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

☐ *Total of _____ forms are submitted.

REMARKS WITH PRE-APPEAL BRIEF REQUEST FOR REVIEW

Claims 8, 9, 14, 15, 18, 19, 23, 24 and 26-45 are rejected under 35 U.S.C. 112, first paragraph. The Examiner suggests that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Pending claims are drawn to a method of imaging a gynecologic cancer comprising contacting a cell with a polyclonal or monoclonal antibody which specifically binds the native protein expressed by SEQ ID NO:1 and detecting bound polyclonal or monoclonal antibody indicative of the presence of a gynecologic cancer; and a method of delivering a derivatized polyclonal or monoclonal antibody to a gynecologic cancer cell comprising administering to the cell a derivatized antibody which specifically binds the native protein expressed by SEQ ID NO:1.

Applicants respectfully direct the reviewers to page 4, lines 23-28, page 7, line 34 through page 8, line 2, and page 14, line 28 through page 16, line 15, wherein it is disclosed that the native protein expressed by the polynucleotide sequence of SEQ ID NO:1 and antibodies thereto are useful in imaging gynecologic cancers. Applicants also respectfully direct the reviewers to pages 17-25 wherein data evidencing measurement of SEQ ID NO:1;Clone ID 145062, Gene ID 236019 ("Pro104") to be a diagnostic marker for ovarian cancer and cervix, endometrium, uterus and mammary cancers.

In addition, Applicants respectfully direct the reviewers to the Information Disclosure Statement submitted March 16, 2005 inclusive of a copy of a poster by Papkoff et al. (Abstract Number A215) presented on November 18, 2003 at the AACR-NCI-

EORTC 2003 International Conference on "Molecular Targets and Cancer Therapeutics discovery, biology, and clinical applications" and a reference by Tang et al. Cancer Res. 2005 65(3):868-878. The Papkoff et al. poster, specifically frames 7 and 8, provides confirmatory data in accordance with teachings of the instant specification that the native protein expressed by the polynucleotide sequence of SEQ ID NO:1 is over-expressed in gynecologic cancer cells as compared to normal tissue, and an antibody which specifically binds the native protein expressed by SEQ ID NO:1 can be used to image gynecologic cancer cells and deliver agents to gynecologic cancer cells as claimed. The Tang et al. reference provides additional confirmatory teachings of testisin (Pro104) being highly expressed in ovarian cancer and premeiotic spermatocytes with relatively little expression in other normal tissues. This reference also teaches that testisin (Pro104) protein expression is consistent with relative mRNA expression and is localized on the surface of cultured tumor cells. Further, data presented in this references demonstrate that testisin (Pro104) can promote cellular processes that drive malignant transformation. The functional data coupled with the restricted normal tissue distribution of testisin and its overexpression in a majority of ovarian cancers taught in these references confirms and validates testisin (Pro104) protein as a diagnostic target and use of testisin (Pro104) antibodies to image gynecologic cancers.

The Examiner has refused to accept this confirming evidence as demonstrating utility of the instant claimed invention suggesting that the specification as originally filed does not teach any protein having 314 amino acids or the protein testisin. Applicants believe this refusal is an error and contradicts recent decisions by the Board of Patent Appeals and Interferences such as Ex Parte Walke et al. (Appeal 2007-3881).

The originally filed specification teaches polynucleotide SEQ ID NO:1, polypeptide SEQ ID NO:2 encoded by the polynucleotide SEQ ID NO:1 and the native protein expressed by the gene comprising the polynucleotide of SEQ ID NO:1. Applicant's claims are directed to the native protein expressed by SEQ ID NO:1. SEQ ID NO:2 depicts in its sequence 13 amino acids before the initial methionine of the native protein expressed by SEQ ID NO:1. These 13 deduced amino acids depicted in SEQ ID NO:2 occur prior to the translation initiation codon in SEQ ID NO:1 and thus do not occur in the native protein expressed by SEQ ID NO:1. The native protein expressed by SEQ ID NO:1 is identical to amino acids 14-327 of SEQ ID NO:2. The 13 amino acids in SEQ ID NO:2 which are upstream of the beginning of the native protein expressed by SEQ ID NO:1 result in the Examiner's suggestion that "instant SEQ ID NO:2 is not the same as testisin". Applicants do not assert SEQ ID NO:2 to be testisin.

However, comparison of the native protein expressed by SEQ ID NO:1 (amino acids 14-327 of SEQ ID NO:2) with testisin shows that the native protein expressed by SEQ ID NO:1 and testisin to be identical.

Further, at page 10 of the Office Action mailed April 21, 2004 the Examiner stated the Office's interpretations to be:

> that the instant SEQ ID NO:1 encodes the art-known protein, lacking the first 13 amino acids of instant SEQ ID NO:2.

In the same Office Action, the Examiner acknowledged that it was known from teachings of Darnell et al. that any in vivo translated protein has Met as the first amino acid and that since SEQ ID NO:2 starts with an Arg it is not the protein expressed in vivo by SEQ ID NO:1. Further, the first ATG of SEQ ID NO:1 and the flanking sequence, GAGGCCATGG, is identifiable

as an translation initiator codon as defined by the eukaryotic Kozak consensus sequence.

Thus, the skilled artisan, upon reading the instant application, would clearly understand the native protein expressed by SEQ ID NO:1 to be amino acids 14 to 327 of SEQ ID NO:2, which is also known as testisin.

Further, the Examiner has failed to meet the burden of showing a reasonable basis for doubting the utility of the claimed invention.

Applicant's submission of Papkoff et al. and Tang et al. clearly rebuts the Examiner's suggestion that in the absence of a disclosure in the specification of a correlation between protein over-expression and over-expression of mRNA levels, the predictability of protein translation is not solely contingent on mRNA expression due to the multitude of homeostatic factors affecting transcription and translation. Submission of these references also confirms Applicants' argument that teachings of Hooper et al. relating to testicular cancer are not relevant to the instant claimed invention.

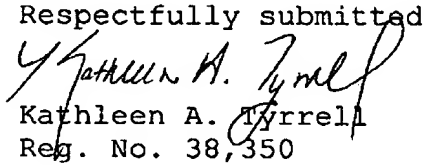
Applicants respectfully direct the reviewers to pages 10-13 of the reply filed August 23, 2004, pages 3-9 of the reply filed March 15, 2005, pages 11-17 of the reply filed July 17, 2006, pages 10-13 of the reply filed February 27, 2007 and pages 2-8 of the reply filed August 18, 2007, wherein additional arguments submitted by Applicants traversing this enablement rejection are set forth.

Applicants believe that similarly to Ex Parte Walke et al. (Appeal 2007-3881), the prosecution history record of the instant application and teachings of the specification establish that those of skill in the art would have understood the specification to disclose the native protein expressed by SEQ ID NO:1 to be the same as testisin and therefore to possess the

same activities. Further, similarly to Ex Parte Walke et al. (Appeal 2007-3881), Applicants believe that prosecution history record establishes that the Examiner has failed to meet her burden of showing that the claimed invention lacks patentable utility. As stated in Ex Parte Walke et al., after the Examiner has challenged the asserted utility of a claimed invention and the Applicant has provided evidence or argument in rebuttal, the merits of the rejection must be re-evaluated in light of all the evidence of record, and patentability determined based on a preponderance of the evidence.

Applicants believe, based upon the evidence provided, that patentability has been established and the rejection under 35 U.S.C. 112, first paragraph should be withdrawn.

Respectfully submitted,



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Date: **February 5, 2008**

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